DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
10903 New Hampshire Avenue
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Silver Spring, MD 20993-0002

June 4, 2015

ORTHO CLINICAL DIAGNOSTICS
BRADLEY BOYER
SENIOR REGULATORY ASSOCIATE
100 INDIGO CREEK DRIVE
ROCHESTER NY 14626

Re: K142595
Trade/Device Name: VITROS Chemistry Products HbA1c Reagent Kit,
VITROS Chemistry Products Calibrator Kit 31,
VITROS Chemistry Products %Alc Performance Verifiers I And II
Regulation Number: 21 CFR 862.1373
Regulation Name: Glycosylated hemoglobin assay
Regulatory Class: II
Product Code: PDJ, JIT, JJY
Dated: April 27, 2015
Received: April 28, 2015

Dear Bradley Boyer:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Parts 801 and 809); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820); and if applicable, the

electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

If you desire specific advice for your device on our labeling regulations (21 CFR Parts 801 and 809), please contact the Division of Industry and Consumer Education at its toll-free number (800) 638 2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm for the CDRH's Office of Surveillance and Biometrics/Division of Postmarket Surveillance.

You may obtain other general information on your responsibilities under the Act from the Division of Industry and Consumer Education at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm.

Sincerely yours,

Katherine Serrano -S

For:

Courtney H. Lias, Ph.D.
Director
Division of Chemistry and Toxicology Devices
Office of In Vitro Diagnostics
and Radiological Health
Center for Devices and Radiological Health

Enclosure

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Indications for Use

Form Approved: OMB No. 0910-0120
Expiration Date: January 31, 2017
See PRA Statement below.

510(k) Number *(if known)*
k142595

Device Name
VITROS Chemistry Products HbA1c Reagent Kit
VITROS Chemistry Products Calibrator Kit 31
VITROS Chemistry Products %A1c Performance Verifiers I and II

Indications for Use *(Describe)*

For in vitro diagnostic use only
VITROS Chemistry Products HbA1c reagent is used on VITROS 5,1 FS Chemistry System, VITROS 4600 Chemistry System and the VITROS 5600 Integrated System for the quantitative determination of percent glycated hemoglobin A1c (DCCT/NGSP) and mmol/mol hemoglobin A1c (IFCC) in human whole blood.
The test is to be used as an aid in diagnosis of diabetes, as an aid in identifying patients who may be at risk for developing diabetes mellitus, and for the monitoring of long-term blood glucose control in individuals with diabetes mellitus.

For in vitro diagnostic use only
VITROS Calibrator Kit 31 is used to calibrate the VITROS 5,1 FS Chemistry System, VITROS 4600 Chemistry System and the VITROS 5600 Integrated System for the determination of percent glycated hemoglobin (HbA1c) in human whole blood.

For in vitro diagnostic use only
VITROS Chemistry Products %A1c Performance Verifiers are assayed controls used on the VITROS 5,1 FS Chemistry System, the VITROS 4600 Chemistry System and the VITROS 5600 Integrated System to monitor performance of the VITROS d%A1c and VITROS HbA1c Reagent Kits.

Type of Use *(Select one or both, as applicable)*

☒ Prescription Use (Part 21 CFR 801 Subpart D) ☐ Over-The-Counter Use (21 CFR 801 Subpart C)

CONTINUE ON A SEPARATE PAGE IF NEEDED.

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510(k) Summary

This summary of 510(k) safety and effectiveness information is being submitted in accordance with the requirements of SMDA 1990 and 21 CFR 807.92.

The assigned 510(k) number is: K142595

1. Submitter Information and Preparation Date

Submitter Name:	Ortho-Clinical Diagnostics, Inc.
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Email:	bboyer@its.jnj.com
Contact Person:	Bradley P. Boyer
Preparation Date:	September 12, 2014. Updated June 3, 2015

2. Device Name

Trade or Proprietary Names:

VITROS® Chemistry Products HbA1c Reagent Kit
VITROS® Chemistry Products Calibrator Kit 31
VITROS® Chemistry Products %A1c Performance Verifiers I and II

Common Names:

HbA1c assay and controls

Classification Names:

Glycosylated Hemoglobin assay (21 CFR 862.1373) Class II
Calibrators (21 CFR 862.1150) Class II
Quality Control material (assayed and unassayed) (21 CFR 862.1660) Class I (general controls). Since these devices (VITROS® %A1c Performance Verifiers I & II) are assayed controls, they meet the reserved criteria under Section 510(l) of the Food, Drug, and Cosmetic Act.

Product Code

PDJ, JJY, JIT

3. Predicate Devices

The VITROS® Chemistry Products HbA1c assay (defined as VITROS® Chemistry Products HbA1c Reagent Kit and VITROS® Chemistry Products Calibrator Kit 31) is substantially equivalent to the Roche Tina Quant HbA1c Dx.Gen.2 assay (K121291).

The VITROS® Chemistry Products Calibrator Kit 31 is substantially equivalent to the Roche C.f.a.s HbA1c (k052101).

The VITROS® Chemistry Products %A1c Performance Verifiers are substantially equivalent to the VITROS® Chemistry Products %A1c Performance Verifiers that were previously cleared (K041764).

4. Device Description

The determination of % glycated hemoglobin (HbA1c) is performed using the VITROS Chemistry Products HbA1c Reagent Kit in conjunction with the VITROS Chemistry Products Calibrator Kit 31 on the VITROS 5,1 FS and VITROS 4600 Chemistry Systems and the VITROS 5600 Integrated System. The VITROS Chemistry Products HbA1c Reagents are two dual chambered packages containing ready-to-use liquid reagents. Whole blood samples are hemolyzed on the VITROS 5,1 FS and VITROS 4600 Chemistry Systems and the VITROS 5600 Integrated System. The concentration of HbA1c and total Hb are measured in the hemolyzed samples, controls and calibrators.

Hemoglobin A1c and Hemoglobin

Whole blood samples are hemolyzed on the VITROS 5,1 FS and VITROS 4600 Chemistry Systems and the VITROS 5600 Integrated System. Calibrators, controls and hemolyzed whole blood samples are mixed with Reagent 1 containing anti-HbA1c antibody to form a soluble antigen-antibody complex. Hemoglobin in the hemolyzed whole blood is converted with Reagent 1 to a hematin derivative that is measured bichromatically at 340 nm and 700 nm. Unbound anti-HbA1c antibody reacts with polyhapten (hexapeptide-glycan, A1c Reagent 2) to form an insoluble antibody-polyhapten immune complex, which is measured turbidimetrically at 340 nm. After a calibration has been performed for each reagent lot, the hemoglobin A1c and Hb

concentrations in each unknown sample can be determined using the stored calibration curves and the measured absorbance obtained in the assay of the hemolyzed sample.

%A1c

%A1c is a derived test calculated from the quantitative measurements of hemoglobin and hemoglobin A1c.

The VITROS® Chemistry Products Calibrator Kit 31 are prepared from a hemolysate derived from human and ovine blood to which surfactants, stabilizer, and preservative have been added. The calibrators are used to calibrate the VITROS 5,1 FS Chemistry System, VITROS 4600 Chemistry System and the VITROS 5600 Integrated System for the determination of percent glycated hemoglobin (HbA1c) in human whole blood.

VITROS %A1c Performance Verifiers I and II are prepared from a hemolysate derived from human and ovine blood to which surfactants, stabilizer, and preservatives have been added.

The VITROS® Chemistry Products FS Reconstitution Diluent is a common reagent that is used by multiple assays on VITROS® 5,1 FS Chemistry Systems, VITROS® 4600 Chemistry Systems, and VITROS® 5600 Integrated Systems. There are no active ingredients, the fluid is proceesed water and is supplied in a 5 mL vial for reconstitution of lyophilized materials.

The VITROS® 5,1 FS Chemistry System and VITROS 4600 Chemistry Systems are clinical chemistry instruments that provide automated use of the VITROS® Chemistry Products MicroTip® and MicroSlides® range of products. The VITROS® 5,1 FS System was cleared for market by 510(k) premarket notification (K031924). The VITROS® 4600 Chemistry System is commercialized under the FDA's Guidance for Industry and Staff: Reagent Replacement and Instrument Family Member Policy (December 11, 2003) as a family member of the VITROS 5,1 FS Chemistry System (K031924). The VITROS® 5600 Integrated Systems are clinical laboratory instruments that provide automated use of the VITROS® Chemistry Products MicroTip® and MicroSlides® range of products and VITROS® Immunodiagnostic Products MicroWells® range of products. The VITROS 5600® Integrated System was cleared for market by 510(k) premarket notification (K081543).

5. Indications for Use

VITROS® Chemistry Products HbA1c Reagent Kit:

For *in vitro* diagnostic use only.

VITROS Chemistry Products HbA1c reagent is used on VITROS 5,1 FS Chemistry System, VITROS 4600 Chemistry System and the VITROS 5600 Integrated System for the quantitative determination of percent glycated hemoglobin A1c (DCCT/NGSP) and mmol/mol hemoglobin A1c (IFCC) in human whole blood. The test is to be used as an aid in diagnosis of diabetes, as an aid in identifying patients who may be at risk for developing diabetes mellitus and for the monitoring of long-term blood glucose control in individuals with diabetes mellitus.

VITROS® Chemistry Products Calibrator Kit 31:

For *in vitro* diagnostic use only.

VITROS Calibrator Kit 31 is used to calibrate the VITROS 5,1 FS Chemistry System, VITROS 4600 Chemistry System and the VITROS 5600 Integrated System for the determination of percent glycated hemoglobin (HbA1c) in human whole blood.

VITROS® Chemistry Products %A1c Performance Verifiers I & II:

For *in vitro* diagnostic use only.

VITROS Chemistry Products %A1c Performance Verifiers are assayed controls used on the VITROS 5,1 FS Chemistry System, the VITROS 4600 Chemistry System and the VITROS 5600 Integrated System to monitor performance of the VITROS d%A1c and VITROS HbA1c Reagent Kits.

6. Comparison of Technological Characteristics to Predicate Device

VITROS® Chemistry Products HbA1c Reagent and VITROS® Chemistry Products Calibrator Kit 31 (HbA1c assay) are substantially equivalent to the COBAS Integra 800 Tina Quant HbA1c Dx.Gen.2 assay (K121291) (predicate device) which was cleared by the FDA for IVD use.

The VITROS® Chemistry Products Calibrator Kit 31 is substantially equivalent to the Roche C.f.a.s HbA1c (k052101).

The VITROS® Chemistry Products %A1c Performance Verifiers I and II are substantially equivalent to the VITROS® Chemistry Products %A1c Performance

Verifiers I and II (K041764) (predicate device) which was cleared by the FDA for IVD use.

Table 1 Similarities and differences of the assays performed using the VITROS® Chemistry Products HbA1c assay and the COBAS Integra 800 Tina Quant HbA1c Dx.Gen.2 assay.

Device Characteristic	**VITROS® HbA1c assay (New device)**	**COBAS Integra 800 Tina Quant HbA1c Dx.Gen.2 assay (Predicate device)**
Intended Use	For in vitro diagnostic use only. VITROS Chemistry Products HbA1c reagent is used on VITROS 5,1 FS Chemistry System, VITROS 4600 Chemistry System and the VITROS 5600 Integrated System for the quantitative determination of percent glycated hemoglobin A1c (DCCT/NGSP) and mmol/mol hemoglobin A1c (IFCC) in human whole blood. The test is to be used as an aid in diagnosis of diabetes and as an aid in identifying patients who may be at risk for developing diabetes mellitus, and for the monitoring of long-term blood glucose control in individuals with diabetes mellitus.	This test is to be used as an aid in diagnosis of diabetes and as an aid in identifying patients who may be at risk for developing diabetes. The COBAS INTEGRA 800 Tina‑quant Hemoglobin A1cDx Gen.2 assay is an in vitro diagnostic reagent system intended for quantitative determination of mmol/mol hemoglobin A1c (IFCC) and % hemoglobin A1c (DCCT/NGSP) in whole blood on the Roche COBAS INTEGRA 800 clinical chemistry analyzer. HbA1c determinations are useful for monitoring of long-term blood glucose control in individuals with diabetes mellitus.
Calibration	Traceable to the IFCC (International Federation of Clinical Chemistry and Laboratory Medicine) Reference Method	Same
Certification	This method is certified by the National Glycohemoglobin Standardization Program (NGSP).	Same

Device Characteristic	VITROS® HbA1c assay (New device)	COBAS Integra 800 Tina Quant HbA1c Dx.Gen.2 assay (Predicate device)
Test Principle	Whole blood samples are lysed. Hemoglobin is converted to a hematin derivative that is measured bichromatically. HbA1c is measured by turbidimetric inhibition. %A1c is derived from the quantitative measurements of hemoglobin and hemoglobin A1c.	Same
Results	The final result is expressed as mmol/mol HbA1c or %A1c (NGSP)	Same
Sample type	EDTA Whole Blood	Li-heparin, Na-heparin, K2-EDTA, K3-EDTA, potassium fluoride/Na2-EDTA, NaF/sodium EDTA and NaF/potassium oxalate
Measuring Range	4-14 %A1c NGSP units 20-130 HbA1c (mmol/mol) SI units	4.3 -24.8 HbA1c%

Table 2 Similarities and differences of the device characteristics between the VITROS® Chemistry Products Calibrator Kit 31 with the predicate device Roche C.f.a.s HbA1c

Device Characteristic	**VITROS® HbA1c assay** **Calibrator Kit 31 (New device)**	**COBAS Integra 800 Tina Quant HbA1c Dx.Gen.2 assay** **C.f.a.s HbA1c calibrator (Predicate device) k052101**
Intended Use	For in vitro diagnostic use only. VITROS Calibrator Kit 31 is used to calibrate the VITROS 5,1 FS Chemistry System, VITROS 4600 Chemistry System and the VITROS 5600 Integrated System for the determination of percent glycated hemoglobin (HbA1c) in human whole blood.	For use in the calibration of the Hemoglobin A1c assay
Levels	1 level diluted automatically by the system to achieve 4 levels	1 level diluted automatically by the system
Traceability	Traceable to the IFCC (International Federation of Clinical Chemistry and Laboratory Medicine) Reference Method	same

Table 3 Similarities and differences of the device characteristics between the VITROS® Chemistry Products %A1c Performance Verifiers I & II with the predicate device VITROS® Chemistry Products %A1c Performance Verifiers I & II

Device Characteristic	**VITROS® %A1c Performance Verifiers (New Device)**	**VITROS® %A1c Performance Verifiers (Predicate Device)**
Analytes Reported	Hb, A1c, %A1c (derived)	Same
Vial Volume	1 mL when reconstituted	Same
Number of vials	3 vials each level	Same
Intended Use	For in vitro diagnostic use only. VITROS Chemistry Products %A1c Performance Verifiers are assayed controls used on the VITROS 5,1 FS Chemistry System, the VITROS 4600 Chemistry System and the VITROS 5600 Integrated System to monitor performance of the VITROS d%A1c and VITROS HbA1c Reagent Kits.	Same, except only for use with the VITROS d%A1c Reagent Kit
Product Type	Assayed Control	Same
Presentation	Lyophillized	Same
Number of levels	Two	Same
Nominal Values	PV I: Hb 14g/dL, HbA1c 0.69g/dL PV II Hb 14g/dL, HbA1c 1.48g/dL	Same

7. Performance Data:

Analytical Performance

a. Method comparison with NGSP device:

A Method Comparison Study (Accuracy) was performed comparing the VITROS® Chemistry Products HbA1c assay with testing in a secondary reference laboratory of the NGSP. The testing followed CLSI Protocol EP9[12] and was performed on each of the VITROS systems.

A total of 357 samples which were within the claimed measuring range of both assays were measured in both the VITROS Chemistry Products HbA1c assay and the secondary reference laboratory assay. The samples were distributed across the range of the assay. The relationship between the two methods was as follows:

VITROS Chemistry Products HbA1c assay = 1.00 x secondary reference laboratory method-0.06 (% NGSP) with a correlation coefficient (r) of 0.996.

On all lots and on all VITROS systems the VITROS HbA1c assay has met the requirements of the National Glycohemoglobin Standardization Program and is traceable to the Diabetes Control and Complications Trial Reference Method.

Bias and % Bias versus the reference method on each VITROS System were calculated at 5.0, 6.5, 8.0 and 12% NGSP and are presented in the following tables along with the calculated %Total Error.

Special Controls require Total Error to be ≤6%. Total error was assessed on each VITROS system.

Deming regression analysis was performed for each of the 3 analyzer types. Total Error values at the requested decision levels are shown.

VITROS 5,1 FS Chemistry System – Deming

	Fluid Type	Decision Level (%NGSP)	Bias (%NGSP)	%Bias	%CV	%TE*	%TE^
VITROS 5,1 FS	Control	5.0	-0.040	-0.798	1.83	4.39	4.36
	Control	6.5	-0.029	-0.447	2.09	4.54	4.52
	Control	8.0	-0.018	-0.228	2.69	5.51	5.50
	Control	12.0	0.011	0.089	2.03	4.08	4.08
	Patient	5.0	-0.040	-0.798	2.21	5.14	5.10
	Patient	6.5	-0.029	-0.447	2.01	4.39	4.37
	Patient	8.0	-0.018	-0.228	1.92	4.00	3.99
	Patient	12.0	0.011	0.089	2.52	5.03	5.04

*TE = |Bias| + 1.96*SD

^%TE = |%Bias| + 1.96*%CV*(1+%Bias)

VITROS 4600 Chemistry System – Deming

	Fluid Type	Decision Level (%NGSP)	Bias (%NGSP)	%Bias	%CV	%TE*	%TE^
VITROS 4600	Control	5.0	-0.040	-0.805	1.19	3.14	3.13
	Control	6.5	-0.011	-0.164	1.62	3.34	3.34
	Control	8.0	0.019	0.236	1.43	3.03	3.04
	Control	12.0	0.098	0.814	2.01	4.75	4.78
	Patient	5.0	-0.040	-0.805	1.10	2.97	2.95
	Patient	6.5	-0.011	-0.164	1.19	2.50	2.49
	Patient	8.0	0.019	0.236	1.66	3.50	3.50
	Patient	12.0	0.098	0.814	2.09	4.91	4.94

*TE = |Bias| + 1.96*SD

^%TE = |%Bias| + 1.96*%CV*(1+%Bias)

VITROS 5600 Integrated System – Deming

	Fluid Type	Decision Level (%NGSP)	Bias (%NGSP)	%Bias	%CV	%TE*	%TE^
VITROS 5600	Control	5.0	-0.036	-0.723	1.41	3.48	3.46
	Control	6.5	-0.030	-0.467	1.40	3.21	3.19
	Control	8.0	-0.024	-0.306	1.27	2.80	2.79
	Control	12.0	-0.009	-0.075	1.76	3.52	3.52
	Patient	5.0	-0.036	-0.723	1.05	2.79	2.77
	Patient	6.5	-0.030	-0.467	1.12	2.66	2.65
	Patient	8.0	-0.024	-0.306	1.28	2.81	2.80
	Patient	12.0	-0.009	-0.075	1.94	3.88	3.88

*TE = |Bias| + 1.96*SD

^%TE = |%Bias| + 1.96*%CV*(1+%Bias)

Summary statistics of the Accuracy study are provided.

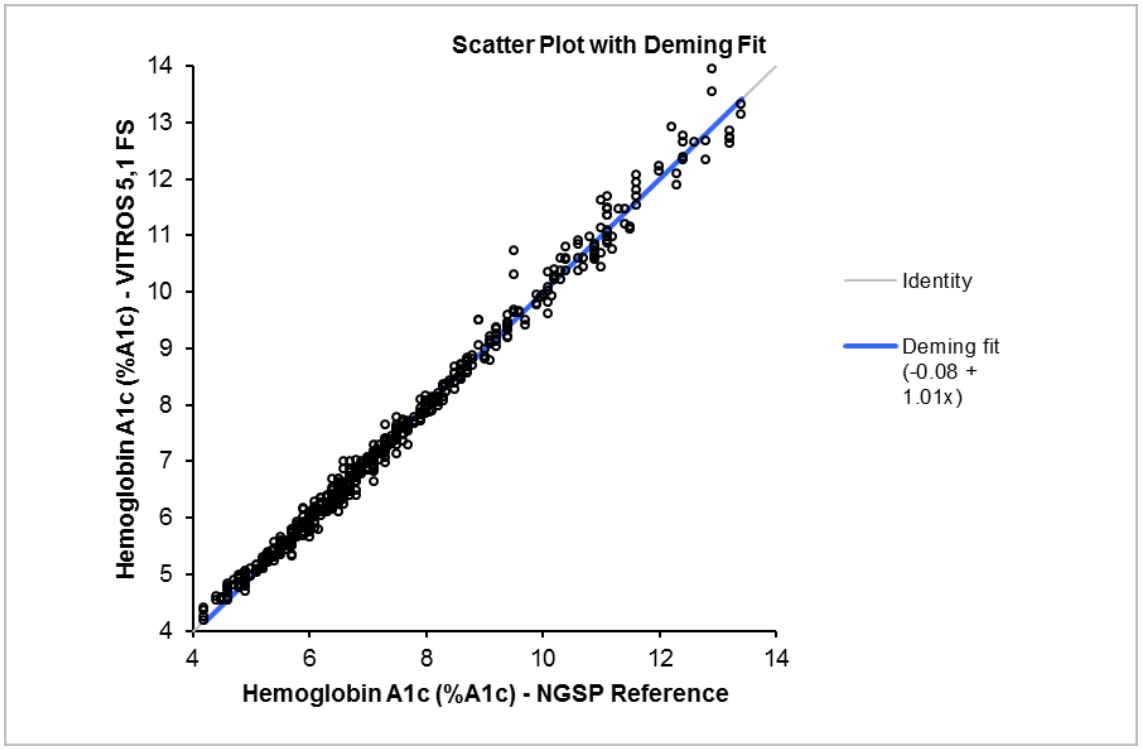
Summary of Accuracy Study Results

	n	Slope	95% CI of Slope	Correlation Coefficient	NGSP Units				HbA1c SI Units (mmol/mol)			
					Range of Sample Conc.	Intercept	95% CI of Intercept	Sy.x	Range of Sample Conc.	Intercept	95% CI of Intercept	Sy.x
5600 vs. comparative method	357	1.00	0.99 - 1.02	0.996	4.2 - 13.4	-0.06	-0.13 - 0.02	0.18	22 - 123	-0.4	-0.9 - 0.2	1.9
4600 vs. comparative method	357	1.02	1.01 - 1.03	0.995	4.2 - 13.4	-0.14	-0.22 - (-0.06)	0.19	22 - 123	-0.9	-1.5 - (-0.3)	2.1
5,1 FS vs. comparative method	357	1.01	0.99 - 1.02	0.996	4.2 - 13.4	-0.08	-0.16 - 0.01	0.18	22 - 123	-0.5	-1.1 - 0.1	1.9
4600 vs. 5600	125	1.00	0.99 - 1.01	0.998	4.3 - 13.1	-0.01	-0.09 - 0.06	0.10	23 - 120	-0.1	-0.7 - 0.4	1.1
5,1 FS vs. 5600	126	0.99	0.97 - 1.00	0.998	4.3 - 13.8	0.01	-0.09 - 0.12	0.12	23 - 127	-0.2	-1.0 - 0.6	1.3

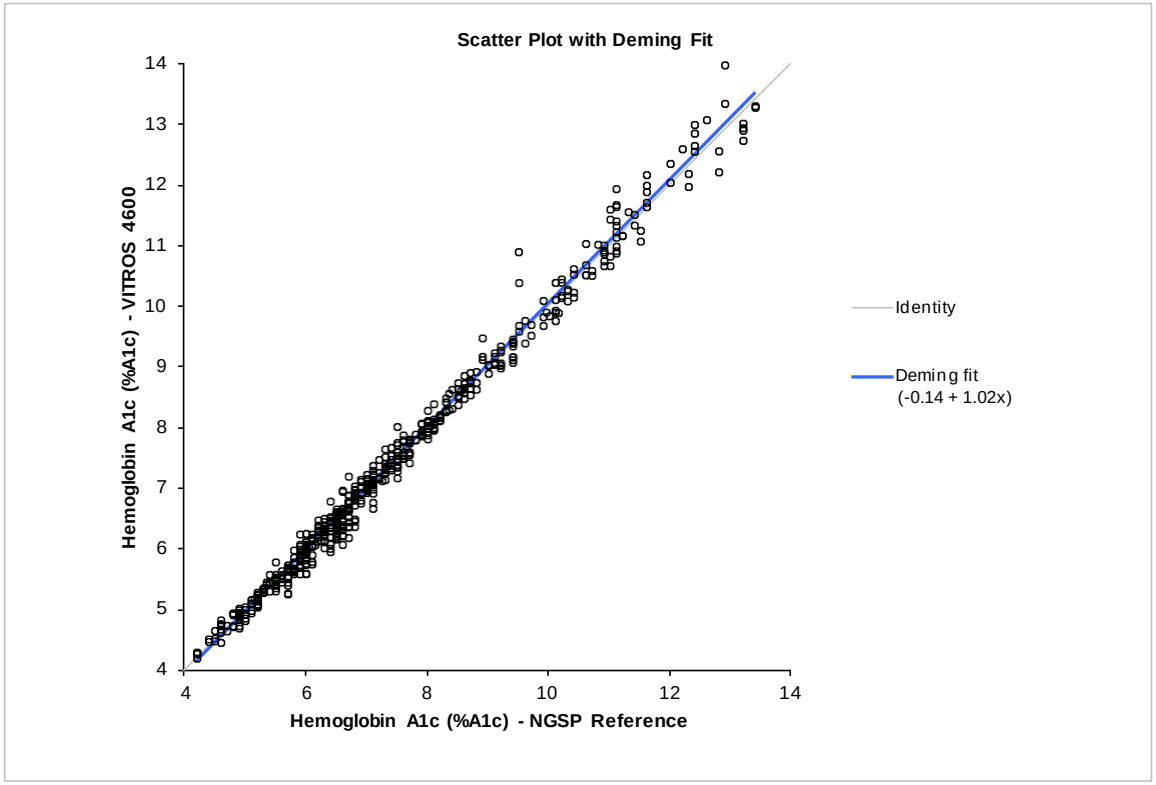
*Secondary Reference Laboratory of the NGSP

Analysis was performed by Deming Regression and Passing-Bablok for each analyzer type. Plots of the Deming regression are shown for each analyzer type and a Summary table is provided below.

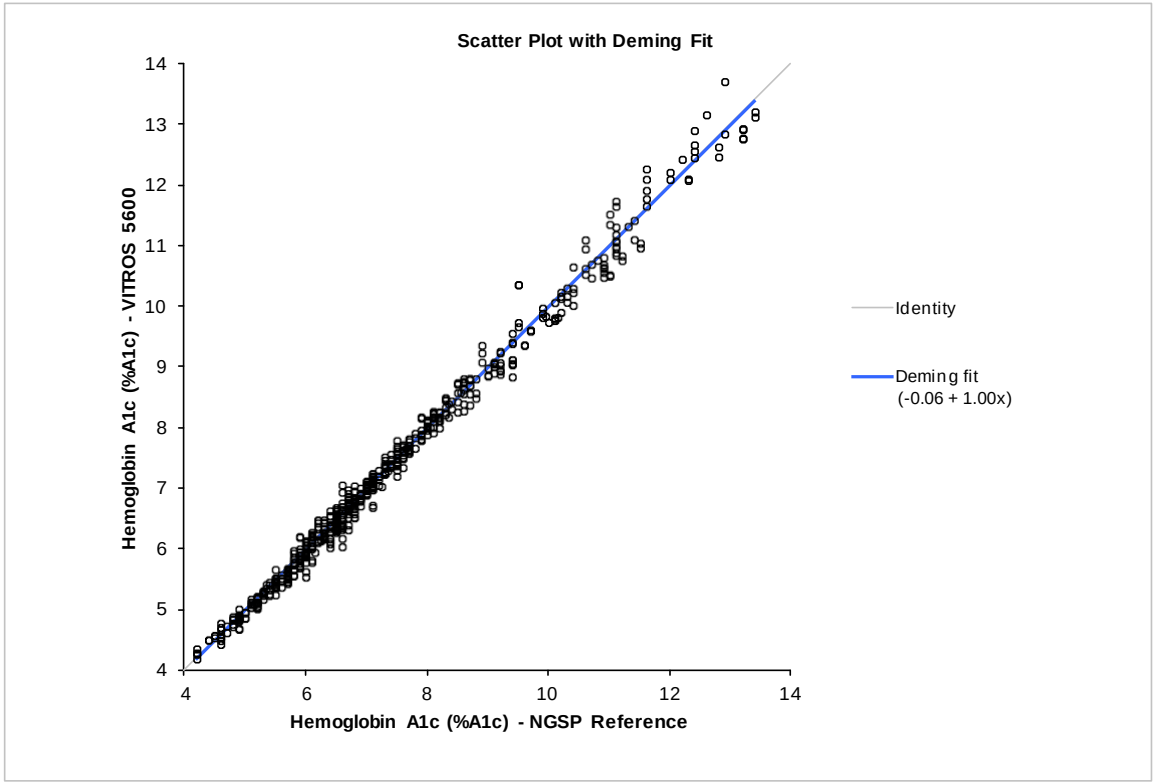
Scatter Plot for the Deming regression on the VITROS 5,1 FS for the combined data



Scatter Plot for the Deming regression on the VITROS 4600 for the combined data



Scatter Plot for the Deming regression on the VITROS 5600 for the combined data



Regression Summary Table Statistics for the combined data for each analyzer family

Analyzer	Regression	Slope	95% CI	Intercept	95% CI
5,1 FS	Passing-Bablok	0.998	0.991 to 1.006	-0.019	-0.072 to 0.031
	Deming	1.007	0.995 to 1.02	-0.076	-0.16 to 0.008
4600	Passing-Bablok	1.012	1.004 to 1.02	-0.079	-0.133 to -0.025
	Deming	1.020	1.007 to 1.032	-0.139	-0.222 to -0.056
5600	Passing-Bablok	1.004	0.996 to 1.011	-0.056	-0.107 to -0.005
	Deming	1.004	0.992 to 1.015	-0.056	-0.132 to 0.021

b. Precision/Reproducibility:

The precision of the VITROS® Chemistry Products HbA1c assay was evaluated on the VITROS 5,1 FS Chemistry System, VITROS 4600 Chemistry System and VITROS 5600 Integrated System following CLSI EP05-A2[13]. The evaluation was conducted on three of each VITROS systems. Three reagent lots were evaluated on each analyzer system. Data were analyzed by Analysis of Variance (ANOVA). Test samples were targeted at 5.0, 6.5, 8.0, and 12.0 % A1c. Precision was evaluated with quality control materials (hemolysate and whole blood-based) for 20-days. An intermediate precision study using whole blood patient samples spanned 4-days. All acceptance criteria for precision were met.

Within Lab precision (Total) was determined using a three lots of reagents on three analyzers on each platform, using a single calibration per lot. Data is shown in both NGSP units and SI units. Results are summarized in the following tables.

Summary of ANOVA Precision Results for VITROS 5,1 FS Chemistry Systems (%A1c, NGSP)

Single Cal				Repeatability		Between Run		Between Day		Between Lot		Between Analyzer		Total	
Fluid	Days	N	Ave	SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
VITROS PV1	21	756	5.65	0.033	0.58%	0.037	0.65%	0.039	0.69%	0.045	0.80%	0.085	1.50%	0.115	2.03%
5% BBI Control	22	792	4.96	0.026	0.52%	0.032	0.64%	0.029	0.58%	0.043	0.87%	0.063	1.27%	0.091	1.83%
6.5% BBI Control	21	756	6.38	0.048	0.75%	0.052	0.82%	0.050	0.78%	0.057	0.89%	0.084	1.32%	0.133	2.09%
8% BBI Control	22	792	8.17	0.065	0.80%	0.041	0.50%	0.065	0.80%	0.081	0.99%	0.178	2.18%	0.220	2.69%
12% BBI Control	20	720	11.85	0.147	1.24%	0.092	0.78%	0.119	1.00%	0.102	0.86%	0.058	0.49%	0.241	2.03%
5% Patient	4	144	5.02	0.023	0.46%	0.031	0.62%	0.032	0.64%	0.033	0.66%	0.094	1.87%	0.111	2.21%
6.5% Patient	4	144	6.51	0.038	0.58%	0.038	0.58%	0.042	0.64%	0.053	0.81%	0.099	1.52%	0.131	2.01%
8% Patient	4	144	8.16	0.054	0.66%	0.071	0.87%	0.031	0.38%	0.064	0.78%	0.107	1.31%	0.157	1.92%
12% Patient	4	144	11.93	0.171	1.43%	0.173	1.45%	0.090	0.75%	0.114	0.96%	0.100	0.84%	0.301	2.52%

Summary of ANOVA Precision Results for VITROS 5,1 FS Chemistry Systems (mmol/mol, SI)

Single Cal				Repeatability		Between Run		Between Day		Between Lot		Between Analyzer		Total	
Fluid	Days	N	Ave	SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
VITROS PV1	21	756	38.3	0.36	0.9%	0.40	1.0%	0.43	1.1%	0.49	1.3%	0.93	2.4%	1.26	3.3%
5% BBI Control	22	792	30.7	0.28	0.9%	0.35	1.1%	0.32	1.0%	0.47	1.5%	0.69	2.2%	0.99	3.2%
6.5% BBI Control	21	756	46.2	0.52	1.1%	0.57	1.2%	0.55	1.2%	0.62	1.3%	0.92	2.0%	1.45	3.1%
8% BBI Control	22	792	65.7	0.71	1.1%	0.45	0.7%	0.71	1.1%	0.89	1.4%	1.95	3.0%	2.40	3.7%
12% BBI Control	20	720	106.0	1.61	1.5%	1.01	1.0%	1.30	1.2%	1.11	1.0%	0.63	0.6%	2.63	2.5%
5% Patient	4	144	31.3	0.25	0.8%	0.34	1.1%	0.35	1.1%	0.36	1.2%	1.03	3.3%	1.21	3.9%
6.5% Patient	4	144	47.7	0.42	0.9%	0.42	0.9%	0.46	1.0%	0.58	1.2%	1.08	2.3%	1.43	3.0%
8% Patient	4	144	65.6	0.59	0.9%	0.78	1.2%	0.34	0.5%	0.70	1.1%	1.17	1.8%	1.72	2.6%
12% Patient	4	144	106.9	1.87	1.7%	1.89	1.8%	0.98	0.9%	1.25	1.2%	1.09	1.0%	3.29	3.1%

Summary of ANOVA Precision Results for VITROS 4600 Chemistry Systems (%A1c, NGSP)

Single Cal				Repeatability		Between Run		Between Day		Between Lot		Between Analyzer		Total	
Fluid	Days	N	Ave	SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
VITROS PV1	21	756	5.63	0.035	0.62%	0.021	0.37%	0.029	0.52%	0.033	0.59%	0.043	0.76%	0.074	1.32%
5% BBI Control	22	792	4.94	0.028	0.57%	0.017	0.34%	0.024	0.49%	0.033	0.67%	0.028	0.57%	0.059	1.19%
6.5% BBI Control	21	756	6.35	0.050	0.79%	0.045	0.71%	0.034	0.54%	0.055	0.87%	0.044	0.69%	0.103	1.62%
8% BBI Control	22	792	8.07	0.071	0.88%	0.037	0.46%	0.046	0.57%	0.043	0.53%	0.054	0.67%	0.115	1.43%
12% BBI Control	20	720	11.89	0.177	1.49%	0.069	0.58%	0.109	0.92%	0.095	0.80%	0.000	0.00%	0.239	2.01%
5% Patient	4	144	4.98	0.027	0.54%	0.025	0.50%	0.016	0.32%	0.012	0.24%	0.036	0.72%	0.055	1.10%
6.5% Patient	4	144	6.47	0.049	0.76%	0.019	0.29%	0.020	0.31%	0.034	0.53%	0.040	0.62%	0.077	1.19%
8% Patient	4	144	8.06	0.090	1.12%	0.064	0.79%	0.032	0.40%	0.052	0.65%	0.044	0.55%	0.134	1.66%
12% Patient	4	144	11.96	0.157	1.31%	0.142	1.19%	0.117	0.98%	0.064	0.54%	0.000	0.00%	0.250	2.09%

Summary of ANOVA Precision Results for VITROS 4600 Chemistry Systems (mmol/mol, SI)

Single Cal				Repeatability		Between Run		Between Day		Between Lot		Between Analyzer		Total	
Fluid	Days	N	Ave	SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
VITROS PV1	21	756	38.0	0.38	1.0%	0.23	0.6%	0.32	0.8%	0.36	0.9%	0.47	1.2%	0.81	2.1%
5% BBI Control	22	792	30.5	0.31	1.0%	0.19	0.6%	0.26	0.9%	0.36	1.2%	0.31	1.0%	0.64	2.1%
6.5% BBI Control	21	756	45.9	0.55	1.2%	0.49	1.1%	0.37	0.8%	0.60	1.3%	0.48	1.0%	1.13	2.5%
8% BBI Control	22	792	64.7	0.78	1.2%	0.40	0.6%	0.50	0.8%	0.47	0.7%	0.59	0.9%	1.26	1.9%
12% BBI Control	20	720	106.5	1.93	1.8%	0.75	0.7%	1.19	1.1%	1.04	1.0%	0.00	0.0%	2.61	2.5%
5% Patient	4	144	30.9	0.30	1.0%	0.27	0.9%	0.17	0.6%	0.13	0.4%	0.39	1.3%	0.60	1.9%
6.5% Patient	4	144	47.1	0.54	1.1%	0.21	0.4%	0.22	0.5%	0.37	0.8%	0.44	0.9%	0.84	1.8%
8% Patient	4	144	64.6	0.98	1.5%	0.70	1.1%	0.35	0.5%	0.57	0.9%	0.48	0.7%	1.46	2.3%
12% Patient	4	144	107.2	1.72	1.6%	1.55	1.4%	1.28	1.2%	0.70	0.7%	0.00	0.0%	2.73	2.5%

Summary of ANOVA Precision Results for VITROS 5600 Integrated Systems (%A1c, NGSP)

Single Cal				Repeatability		Between Run		Between Day		Between Lot		Between Analyzer		Total	
Fluid	Days	N	Ave	SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
VITROS PV1	21	756	5.66	0.036	0.64%	0.013	0.23%	0.020	0.35%	0.031	0.55%	0.041	0.72%	0.067	1.18%
5% BBI Control	22	792	4.98	0.034	0.68%	0.011	0.22%	0.017	0.34%	0.058	1.17%	0.000	0.00%	0.070	1.41%
6.5% BBI Control	21	756	6.37	0.057	0.90%	0.029	0.46%	0.034	0.53%	0.033	0.52%	0.041	0.64%	0.089	1.40%
8% BBI Control	22	792	8.10	0.072	0.89%	0.017	0.21%	0.030	0.37%	0.054	0.67%	0.037	0.46%	0.103	1.27%
12% BBI Control	20	720	11.89	0.178	1.50%	0.055	0.46%	0.067	0.56%	0.018	0.15%	0.066	0.56%	0.209	1.76%
5% Patient	4	144	5.04	0.027	0.54%	0.013	0.26%	0.021	0.42%	0.032	0.64%	0.020	0.40%	0.053	1.05%
6.5% Patient	4	144	6.53	0.042	0.64%	0.026	0.40%	0.019	0.29%	0.038	0.58%	0.032	0.49%	0.073	1.12%
8% Patient	4	144	8.14	0.062	0.76%	0.062	0.76%	0.000	0.00%	0.044	0.54%	0.032	0.39%	0.104	1.28%
12% Patient	4	144	12.04	0.173	1.44%	0.089	0.74%	0.088	0.73%	0.064	0.53%	0.070	0.58%	0.234	1.94%

Summary of ANOVA Precision Results for VITROS 5600 Integrated Systems (mmol/mol, SI)

Single Cal				Repeatability		Between Run		Between Day		Between Lot		Between Analyzer		Total	
Fluid	Days	N	Ave	SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
VITROS PV1	21	756	38.4	0.39	1.0%	0.14	0.4%	0.22	0.6%	0.34	0.9%	0.45	1.2%	0.73	1.9%
5% BBI Control	22	792	30.9	0.37	1.2%	0.12	0.4%	0.19	0.6%	0.63	2.0%	0.00	0.0%	0.77	2.5%
6.5% BBI Control	21	756	46.1	0.62	1.3%	0.32	0.7%	0.37	0.8%	0.36	0.8%	0.45	1.0%	0.97	2.1%
8% BBI Control	22	792	65.0	0.79	1.2%	0.19	0.3%	0.33	0.5%	0.59	0.9%	0.40	0.6%	1.13	1.7%
12% BBI Control	20	720	106.4	1.95	1.8%	0.60	0.6%	0.73	0.7%	0.20	0.2%	0.72	0.7%	2.28	2.1%
5% Patient	4	144	31.5	0.30	1.0%	0.14	0.4%	0.23	0.7%	0.35	1.1%	0.22	0.7%	0.58	1.8%
6.5% Patient	4	144	47.8	0.46	1.0%	0.28	0.6%	0.21	0.4%	0.42	0.9%	0.35	0.7%	0.80	1.7%
8% Patient	4	144	65.4	0.68	1.0%	0.68	1.0%	0.00	0.0%	0.48	0.7%	0.35	0.5%	1.14	1.7%
12% Patient	4	144	108.1	1.89	1.7%	0.97	0.9%	0.96	0.9%	0.70	0.6%	0.77	0.7%	2.56	2.4%

c. Linearity/assay measuring range:

Evaluation of the linearity of the VITROS® Chemistry Products HbA1c assay was performed based on CLSI EP06-A[14]. For each assay component (Hb, HbA1c, %A1c), a low pool and a high pool were prepared with the assay component near the extremes of the calibration range. The low and high concentration pools were mixed to give 16 further pools of intermediate concentrations. The VITROS HbA1c assay was tested using each VITROS System. The VITROS HbA1c assay is linear through the following ranges:

Linear range for Hb: 4.972 – 30.318 g/dL (component) Linear range for HbA1c: 0.080 – 2.530 g/dL (component) Linear range for %A1c: 3.034–15.444% (NGSP derived test) Linear range for HbA1c: 9.6-145.3 mmol/mol (SI derived test)

For each test component, the linearity passes the Acceptance Criteria and presents acceptable performance.
The linearity results support a measuring range of the VITROS HbA1c assay from 4% to 14% (alternate units: 20-130 mmole/mol).

Regression Statistics for the Linearity Assessment
%HbA1c, NGSP

Analyzer	Intercept	Slope	r^2	Concentration Range Tested
VITROS 5,1 FS	0.005	0.9995	0.999	2.39 to 17.35 %HbA1c
VITROS 4600	0.030	0.9957	0.997	3.03 to 15.44 %HbA1c
VITROS 5600	0.012	0.9988	0.999	2.89 to 15.79 %HbA1c

mmol/mol, SI

Analyzer	Intercept	Slope	r^2	Concentration Range Tested
VITROS 5,1 FS	0.044	0.9995	0.999	2.6 to 166.1 mmol/mol
VITROS 4600	0.223	0.9957	0.997	9.6 to 145.3 mmol/mol
VITROS 5600	0.099	0.9988	0.999	8.1 to 149.1 mmol/mol

d. Detection limit: Limit of Blank, Limit of Detection, Limit of Quantitation

Limits of Detection and Quantitation were evaluated following CLSI document EP17-A2[15]. The VITROS® Chemistry Products HbA1c assay was tested using eachVITROS System. Separate evaluations were performed for Hb, HbA1c and the derived test %A1c.

The Limit of Blank, Limit of Detection and Limits of Quantitation were conservatively selected as the Lot/Analyzer yielding the highest values and are summarized in the following tables.

Limit of Blank, Limit of Detection and Limit of Quantitation – Hb

LoB		LoD*		LoQ	
g/dL	g/L	g/dL	g/L	g/dL	g/L
0.186	1.86	0.312	3.12	2.117	21.17

*Proportions of false positives (α) and false negatives (β) were less than 5%; based on 500 determinations, with 5 low-level samples.

Limit of Blank, Limit of Detection and Limit of Quantitation – HbA1c

LoB		LoD*		LoQ	
g/dL	g/L	g/dL	g/L	g/dL	g/L
0.042	0.42	0.072	0.72	0.133	1.33

*Proportions of false positives (α) and false negatives (β) were less than 5%; based on 500 determinations, with 5 low-level samples.

Limit of Blank, Limit of Detection and Limit of Quantitation – %A1c

LoB		LoD*		LoQ	
NGSP	SI (mmol/mol)	NGSP	SI (mmol/mol)	NGSP	SI (mmol/mol)
2.396	2.67	2.580	4.68	2.580	4.68

*Proportions of false positives (α) and false negatives (β) were less than 5%; based on 500 determinations, with 5 low-level samples.

In all cases (Hb component, HbA1c component and %A1c derived test), the determined LoQ met the acceptance criteria and supports a LoQ claim of 2.580% NGSP.

e. Dilution Study:

On-Analyzer dilution is not supported.

f. Traceability

Traceability of the Calibration: The values assigned to the VITROS® Chemistry Products Calibrator Kit 31 for %A1c are traceable to the IFCC (International Federation of Clinical Chemistry and Laboratory Medicine) Reference Method[1]. The derived result (%A1c) is calculated from the individual quantitative results for hemoglobin (Hb) and glycated hemoglobin (HbA1c). NGSP results are derived from the International Federation of Clinical Chemistry (IFCC) HbA1c

(mmol/mol) SI units using the Master Equation; %NGSP = (0.09148 x IFCC) + 2.152.

g. Analytical specificity:
The effect of potential interferents on the performance of the VITROS Chemistry Products HbA1c assay was assessed using methods based on the guidelines from CLSI EP7-A2[16]. Potential interferents were evaluated on each of the VITROS Systems.

For each substance tested the control pool and the test substance pool replicates were tested with the VITROS HbA1c assay and results compared.

For HbA0, HbA1a, HbA1b, HbC, HbD, HbE, HbF and HbS, patient samples were tested with the VITROS HbA1c assay. The patient samples were also analyzed by a reference method.

Specificity

Substances That Do Not Interfere

- Samples containing hemoglobin variants HbS up to 41%, HbC up to 38%, HbD up to 38% and HbE up to 26% of the total hemoglobin concentration do not interfere.
- The anti-HbA1c antibodies used in this kit do not cross-react with HbA0 up to 90%, HbA1a up to 1.5%, HbA1b up to 4% of the total hemoglobin concentration.
- This method is unaffected by the presence of acetylated hemoglobin, carbamylated hemoglobin, and labile glycated hemoglobin when samples were treated with 50 mg/dL Acetaldehyde, 150 mg/dL Urea, and 1500 mg/dL Glucose for four hours at 37° C, respectively.
- The substances listed in this table were tested with the VITROS Chemistry Products HbA1c assay at %A1c values of approximately 6.5% and 8.5% (48 and 69 HbA1c (mmol/mol)), using protocols based on CLSI Protocol EP7[16] and found not to interfere, bias ≤ 0.5 %A1c and ≤ 0.6 %A1c (≤ 5 and ≤ 7 HbA1c (mmol/mol)), at the concentration shown.

Summary of Interferent testing

Substance*	Concentration	
Acetaminophen	20 mg/dL	1.32 mmol/L
Acetylsalicylic acid	100 mg/dL	5.55 mmol/L
Ampicillin	100 mg/dL	2.86 mmol/L
Ascorbic acid	80 mg/dL	4.54 mmol/L
Bilirubin	50 mg/dL	0.86 mmol/L
Ca-dobesilate	20 mg/dL	0.48 mmol/L
Cefoxitin sodium	250 mg/dL	5.56 mmol/L
Cholesterol	350 mg/dL	9.1 mmol/L
Cyclosporin	0.5 mg/dL	4.16 µmol/L
Doxycyclin hyclate	5 mg/dL	0.10 mmol/L
Glucose	1000 mg/dL	55.5 mmol/L
Glycated Albumin	500 mg/dL	0.07 mmol/L
Ibuprofen	50 mg/dL	2.42 mmol/L
Insulin	592.8 µIU/mL	3926 pmol/L
Intralipid	500 mg/dL	Not Applicable
Levodopa	2 mg/dL	0.10 mmol/L
Metformin	4 mg/dL	0.31 mmol/L
Methyldopa	2 mg/dL	94.7 µmol/L
Metronidazole	20 mg/dL	1.17 mmol/L
N-Acetylcysteine	166.3 mg/dL	10.2 mmol/L
Phenylbutazone	40 mg/dL	1.30 mmol/L
Rheumatoid Factor	750 IU/mL	750 kIU/L
Rifampicin	6 mg/dL	72.9 µmol/L
Rosiglitazone maleate	0.8 mg/dL	16.9 µmol/L
Theophylline	10 mg/dL	0.56 mmol/L
Total Protein	5 g/dL	50 g/L
Total Protein	9 g/dL	90 g/L
Triglyceride	500 mg/dL	5.7 mmol/L

Hb Variant Test Concentration Ranges, %A1c Concentration Range and %A1c Bias - VITROS 5,1 FS

5,1 FS Analyzer							
Hemoglobin Variant	# samples tested	Variant Concentration Range (%)	Range of %A1c Concentration	Relative % Difference from Reference Concentration at Low and High HbA1c Concentrations			
				~ 6.0 %HbA1c		~ 9.0 %HbA1c	
				Relative %Bias	Range %Bias	Relative %Bias	Range %Bias
HbA0	70	49.3 – 90.4	5.8 – 13.4	-1.11	-6.15% to 2.91%	-0.90	-1.93% to 2.04%
HbA1a		0.1 – 1.5					
HbA1b		1.3 – 4.1					
HbA2	22*	4.9 – 6.1	5.7 – 9.0	-1.80	-7.25% to 0.68%	-2.67	-5.08% to -2.13%
HbC	31^	24.5-38.4	5.1 – 9.8	-2.56	-7.13% to 3.24%	-2.85	-4.00% to 0.30%
HbD	21	29.0-38.0	5.2 – 11.3	-1.52	-7.65% to 2.86%	-2.95	-4.34% to 0.05%
HbE	30*	14.3-26.3	5.4 – 9.1	-0.37	-6.45% to 3.95%	-1.00	-1.26% to 6.01%
HbS	40	28.2-41.6	4.6 – 12.7	0.76	-4.72% to 5.95%	0.70	-1.60% to 7.86%
HbF	43	0.2 - 34.8	5.5 - 12.8	-5.31	-29.17% to 2.65%	-2.58	-24.47% to 1.85%

*All twenty-two HbA2 patient samples were spiked.
^Nineteen native HbC patient samples and 12 spiked patient samples
*Eighteen native HbE patient samples and 12 spiked patient samples

Hb Variant Test Concentration Ranges, %A1c Concentration Range and %A1c Bias - VITROS 4600

4600 Analyzer							
Hemoglobin Variant	# samples tested	Variant Concentration Range (%)	Range of %A1c Concentration	Relative % Difference from Reference Concentration at Low and High HbA1c Concentrations			
				~ 6.0 %HbA1c		~ 9.0 %HbA1c	
				Relative %Bias	Range %Bias	Relative %Bias	Range %Bias
HbA0	70	49.3 – 90.4	5.8 – 13.4	-0.91	-6.91% to 4.53%	-0.58	-0.52% to 3.07%
HbA1a		0.1 – 1.5					
HbA1b		1.3 – 4.1					
HbA2	22*	4.9 – 6.1	5.7 – 9.0	-1.78	-7.07% to 1.60%	-1.81	-4.52% to -1.40%
HbC	31^	24.5-38.4	5.1 – 9.8	-1.92	-6.44% to 2.68%	-2.67	-2.58% to -0.26%
HbD	21	29.0-38.0	5.2 – 11.3	-1.33	-6.09% to 1.25%	-3.74	-4.61% to -2.58%
HbE	30*	14.3-26.3	5.4 – 9.1	2.38	-3.41% to 7.92%	-0.69	-5.13% to 1.46%
HbS	40	28.2-41.6	4.6 – 12.7	-0.84	-4.07% to 4.29%	0.30	-1.05% to 7.85%
HbF	43	0.2 - 34.8	5.5 - 12.8	-4.88	-28.65% to 4.29%	-2.63	-23.35% to 2.14%

*All twenty-two HbA2 patient samples were spiked.
^Nineteen native HbC patient samples and 12 spiked patient samples
*Eighteen native HbE patient samples and 12 spiked patient samples

Hb Variant Test Concentration Ranges, %A1c Concentration Range and %A1c Bias - VITROS 5600

5600 Analyzer							
Hemoglobin Variant	# samples tested	Variant Concentration Range (%)	Range of %A1c Concentration	Relative % Difference from Reference Concentration at Low and High HbA1c Concentrations			
				~ 6.0 %HbA1c		~ 9.0 %HbA1c	
				Relative %Bias	Range %Bias	Relative %Bias	Range %Bias
HbA0	70	49.3 – 90.4	5.8 – 13.4	0.06	-5.83% to 4.53%	0.03	0.03% to 2.79%
HbA1a		0.1 – 1.5					
HbA1b		1.3 – 4.1					
HbA2	22*	4.9 – 6.1	5.7 – 9.0	-3.25	-8.12% to 1.33%	-4.12	-8.03% to -1.66%
HbC	31^	24.5-38.4	5.1 – 9.8	-2.86	-6.46% to 1.18%	-3.52	-4.05% to -1.26%
HbD	21	29.0-38.0	5.2 – 11.3	-2.71	-7.18% to 0.45%	-5.37	-6.65% to -4.98%
HbE	30*	14.3-26.3	5.4 – 9.1	-0.49	-6.15% to 3.94%	-2.39	-7.11% to -0.62%
HbS	40	28.2-41.6	4.6 – 12.7	-0.74	-7.40% to 4.24%	-1.87	-1.83% to 4.21%
HbF	43	0.2 - 34.8	5.5 - 12.8	-4.30	-30.03% to 4.24%	-2.03	-25.67% to 2.06%

*All twenty-two HbA2 patient samples were spiked.
^Nineteen native HbC patient samples and 12 spiked patient samples
*Eighteen native HbE patient samples and 12 spiked patient samples

The hemoglobin variants HbA0, HbA1a, HbA1b, C, D, E and S tested over the variant concentration ranges shown do not interfere in this assay.

Known Interferenents:
Glycated HbF is not detected as it does not contain the glycated β-chain that characterizes %A1c. However, HbF is measured in the total Hb assay and as a consequence, specimens containing high amounts of HbF (>7%) may result in lower than expected mmol/mol HbA1c values (IFCC) and %A1c values (NGSP).

h. Reference interval
The expected normal HbA1c range in adults is 4.0-6.0% (NGSP) or 20-42 mmol/mol (IFCC units)[1]. Each laboratory should confirm the validity of these intervals for the population it serves. The Standards of Medical Care in Diabetes - 2015 recommend to diagnose diabetes using a HbA1c method that is NGSP-certified and standardized to the DCCT assay and a cut point of HbA1c ≥ 6.5%.[2,3]

	Current*	**IFCC traceable methods**
Reference interval (non-diabetics)	4–6%	20–42 mmol/mol

*Refer to methods aligned to the US National Glycohemoglobin Standardization Program.

To provide clinical decision guidance for laboratories reporting results in %A1c (NGSP units), the NGSP interval was published by the National Glycohemoglobin Standardization Program (NGSP)[2]. The reference interval is applicable to methods traceable to the Diabetes Control and Complications Trial (DCCT).[4]

%A1c (NGSP)	**Interpretation**
≥ 6.5	Action Suggested

To provide clinical decision guidance for laboratories reporting results in HbA1c mmol/mol (SI units), the following values were calculated from the NGSP %A1c cut point using the Master Equation[5,6]. The HbA1c cut point is ≥ 48 mmol/mol (SI Units).

Calculated HbA1c (mmol/mol) SI Units	**Interpretation**
≥ 48	Action Suggested

References for updated section h - Reference Interval

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5. Hanas R, John G., on behalf of the International HbA1c Consensus Committee. 2010 Consensus Statement on the Worldwide Standardization of the Hemoglobin A1c Measurement. Clin. Chem., 56: 1362 – 1364, 2010.
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i. Antigen Excess.
The potential effect of antigen excess was assessed using fluids that were created from a commercial hemolysate fluid with concentrations through and beyond the assay measuring range for the Hb and the HbA1c components. Samples of each fluid were measured on each VITROS System. No effect from antigen excess was observed for the Hb component for concentrations up to 313.3 g/dL or for the HbA1c component for concentrations up to 21.8 g/dL.

j. NGSP Certification

In accordance with the Special Controls, NGSP certification was received for the VITROS HbA1c assay on the VITROS 5,1 FS Chemistry System, VITROS 4600 Chemistry System and the VITROS 5600 Integrated System.

9. Conclusions

The data presented in the premarket notification provide a reasonable assurance that the VITROS® Chemistry Products HbA1c Reagent Kit, VITROS® Chemistry Products Calibrator Kit 31 and the VITROS® Chemistry Products %A1c Performance Verifiers I and II are safe and effective for the stated intended uses and are substantially equivalent to the cleared predicate devices. Performance was demonstrated with patient samples.